Commissioner is authorized to deduct the fees from Howrey Simon Arnold & White, LLP Deposit Account No. 01-2508/13240.0004.NPUS00/BNT.

For the Examiner's convenience, a list of currently pending claims is attached at the end of this document.

I. Rejection under 35 U.S.C. § 112, first paragraph

Claims 4 and 14 were rejected under 35 U.S.C. § 112, first paragraph, as the specification allegedly does not enable the use of any HMG-1 or HMG-2 family protein. The Examiner indicated that the specification is enabling for the use of human HMG-1 and HMG-2 (SEQ ID NOS:1 and 2).

Applicant asserts that the specification enables one of skill in the art to use HMG-1 and HMG-2 proteins having the described percent sequence homology in the methods of the pending claims.

As described in specification (see Figures 15 and 16) and in the Response filed on May 31, 2002, the HMG-1 and HMG-2 sequences obtained from the various organisms have at least about 90% or 80% sequence homology with SEQ ID NOS:1 and 2, respectively.

The sequence listing provides HMG-1 sequences from human (SEQ ID NO:1), bovine (SEQ ID NO:3), porcine (SEQ ID NO:4), and rat (SEQ ID NO:5). These all have at least about 90% sequence homology with SEQ ID NO:1.

The sequence listing further provides HMG-2 sequences from human (SEQ ID NO:2), porcine (SEQ ID NO:6), bovine (SEQ ID NO:7), rat (SEQ ID NO:8), chicken (SEQ ID NO:9), and mouse (SEQ ID NO:11). These all have at least about 80% sequence homology with SEQ ID NO:2.

The specification at Examples 9 and 10 shows that both human, porcine, and bovine HMG-1 and HMG-2 react with antibodies from ulcerative colitis patients. This is visually shown in Figure 7, lanes 2-5. The immunoassay showed two distinct bands for each of the protein-antibody complexes.

Example 11 describes the detection of anti-HMG-1 and anti-HMG-2 antibodies in ulcerative colitis patients using a mixture of bovine HMG-1 and HMG-2. This is visually shown in Figure 9, where two bands appear in lanes for ulcerative colitis patients, and no bands are visible in lanes for healthy people.

Example 12 describes the detection of anti-HMG-1 and anti-HMG-2 antibodies in refractory ulcerative colitis patients using a mixture of porcine HMG-1 and HMG-2. This is visually shown in Figure 10, where four of five patients tested positive for the antibodies. No antibodies were detected in the sera obtained from healthy people.

Example 13 details the quantitative measurement of anti-HMG-1 and anti-HMG-2 antibodies using bovine HMG-1 and HMG-2 in an ELISA assay.

Example 14 compares the use of human and porcine HMG-1 and HMG-2 in an ELISA assay. In both cases, dosage-dependent straight lines were obtained as calibration curves, indicating that the different proteins can be successfully used in quantitative ELISA assays.

Example 15 shows the measurement of anti-HMG-1 and anti-HMG-2 antibodies in sera obtained from AIH, hepatitis B, and hepatitis C patients. Porcine HMG-1 and HMG-2 were used as antigens. Table 4 on page 49 shows the percentage of positive patients by antigen and by disease. No positives were observed with sera obtained from healthy people. Additionally, AIH and hepatitis C was found to be diagnosed with higher sensitivity using the inventive methods than with an antinuclear antibody assay.

Example 16 details ELISA assays applied to patients having rheumatoid arthritis, systemic lupus erythematosus, Sjögren's syndrome, Behçet's disease, polymyositis / dermatomyositis, scleroderma, primary biliary cirrhosis, microscopic polyangiitis / polyarteritis nodosa, ulcerative colitis, and Crohn's disease. Porcine HMG-1 and HMG-2 were used as antigens. The results of the assays were presented in Table 5.

The specification clearly established that sequences other than human HMG-1 and HMG-2 (SEQ ID NOS:1 and 2) can be used in the claimed methods. The Examples and Figures would lead one of ordinary skill in the art to conclude that HMG-1 proteins having at least about 90% sequence homology with SEQ ID NO:1, and HMG-2 proteins having at least about 80% sequence homology with SEQ ID NO:2 would be operable in the claimed invention.

The mouse HMG-1 and chicken HMG-1 sequences have been removed from claims 6 and 16. Applicant respectfully requests that the rejections of claims 4 and 14 under 35 U.S.C. § 112, first paragraph be withdrawn.

II. Rejection under 35 U.S.C. § 112, second paragraph

Claims 6 and 16 were rejected under 35 U.S.C. § 112, second paragraph as being allegedly indefinite in claiming the subject matter of the invention.

Claims 6 and 16 have been amended to address the Examiner's concerns expressed in the Final Office Action, and do not broaden the scope of the independent claims.

Applicant asserts that claims 6 and 16 are clear and definite. Applicant respectfully requests that the rejections of claims 6 and 16 under 35 U.S.C. § 112, second paragraph be withdrawn.

In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding objections and rejections are respectfully requested. All amendments are made in a good faith effort to advance the prosecution on the merits. Applicant respectfully submits that no amendments have been made to the pending claims for the purpose of overcoming any prior art rejections that would restrict the literal scope of the claims or equivalents thereof. Applicant reserves the right to subsequently take up prosecution of the claims originally filed in this application in continuation, continuation-in-part, and/or divisional applications.

The Examiner is encouraged to call the undersigned should any further action be required for allowance.

Respectfully submitted,

Christopher J. Buntel, Ph.D.
Reg. No. 44,573
Customer No. 23369
ATTORNEY FOR ASSIGNEE,
KANEKA CORPORATION

Howrey Simon Arnold & White, LLP
750 Bering Drive
Houston, TX 77057-2198
(713) 787-1569

August 7, 2002

Marked up version of rewritten claims amended in this Response

4. (Four Times Amended) A kit for diagnosing an autoimmune disease, the kit comprising:

a first antigen [comprising a human HMG-1 polypeptide,] selected from the group consisting of a polypeptide having an amino acid sequence homology of 90% or more with [human HMG-1 indicated by] SEQ ID NO:1, [or] and a fragment [thereof which reacts] of said polypeptide, wherein said polypeptide or fragment thereof specifically binds with an antibody from an autoimmune disease patient;

a second antigen [comprising a human HMG-2 polypeptide,] selected from the group consisting of a polypeptide having an amino acid sequence homology of 80% or more with [human HMG-2 indicated by] SEQ ID NO:2, [or] and a fragment [thereof which reacts] of said polypeptide, wherein said polypeptide or fragment thereof specifically binds with an antibody from an autoimmune disease patient;

a first component for detecting a first antigen-antibody complex; and

a second component for detecting a second antigen-antibody complex; wherein the autoimmune disease is selected from the group consisting of rheumatoid arthritis, human systemic lupus erythematosus, Sjögren's syndrome, Behçet's disease, primary biliary cirrhosis, microscopic polyangitis/polyarteritis nodosa, ulcerative colitis, Chrohn's disease and autoimmune hepatitis.

6. (Twice Amended) The kit of claim 4, wherein:

the polypeptide [from an HMG-1 family] having an amino acid sequence homology of 90% or more with SEQ ID NO:1 is selected from human, bovine, porcine, [chicken, mouse,] or rat HMG-1; and

the polypeptide [from an HMG-2 family] having an amino acid sequence homology of 90% or more with SEQ ID NO:2 is selected from human, bovine, porcine, chicken, mouse, or rat HMG-2.

14. (Twice Amended) A diagnostic drug for detecting an antibody of autoimmune diseases, wherein: the drug comprises:

[a human HMG-1 polypeptide,] a polypeptide having an amino acid sequence homology of 90% or more with [human HMG-1 indicated by] SEQ ID NO:1, or a fragment [thereof which reacts] of said polypeptide, wherein said polypeptide or fragment

thereof specifically binds with an antibody from an autoimmune disease patient; or

[a human HMG-2 polypeptide,] a polypeptide having an amino acid sequence homology of 80% or more with [human HMG-2 indicated by] SEQ ID NO:2, or a fragment [thereof which reacts] of said polypeptide, wherein said polypeptide or fragment thereof specifically binds with an antibody from an autoimmune disease patient;

[the drug reacts with an antibody of an autoimmune disease patient; and]

wherein the autoimmune disease is selected from the group consisting of rheumatoid arthritis, human systemic lupus erythematosus, Sjögren's syndrome, Behçet's disease, primary biliary cirrhosis, microscopic polyangitis/polyarteritis nodosa, ulcerative colitis, Chrohn's disease and autoimmune hepatitis.

16. (Amended) The diagnostic drug of claim 14, wherein:

the polypeptide having an amino acid sequence homology of 90% or more with SEQ ID NO:1 is human HMG-1, [human HMG-2,] bovine HMG-1, [bovine HMG-2,] porcine HMG-1, [porcine HMG-2, chicken HMG-1, chicken HMG-2, mouse HMG-1, mouse HMG-2,] or rat HMG-1[, or rat HMG-2]; and

the polypeptide having an amino acid sequence homology of 80% or more with SEQ ID NO:2 is human HMG-2, bovine HMG-2, porcine HMG-2, chicken HMG-2, mouse HMG-2, or rat HMG-2.